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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/166,649	10/05/1998	ANN MARIE SCHMIDT	56613-JPW/JM	9377

7590 03/10/2003

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EXAMINER
O HARA, EILEEN B

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 03/10/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/166,649	SCHMIDT ET AL.	
	Examiner	Art Unit	
	Eileen O'Hara	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 January 2003 and 24 June 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1,2,4-8,11-13,15,17,18,20-22 and 24-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,5-8,11-13,15,17,18,20-22 and 24-29* is/are rejected.

7)☒ Claim(s) *4* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *See Continuation Sheet* .

Continuation of Attachment(s) 6). Other: CRF Problem Report and Notice to Comply.

DETAILED ACTION

Continued Prosecution Application

1. The request filed on January 27, 2003 for a Continued Prosecution Application (CPA) under 37 CFR 1.53(d) based on parent Application No. 09166,649 is acceptable and a CPA has been established. An action on the CPA follows.

Status of Claims

2. Claims 1, 2, 4-8, 11-13, 15, 17, 18, 20-22 and 24-29 are pending and under examination in the instant application. Claim 29 has been amended as requested by Applicant in Paper Number 16, filed June 24, 2002.

Election/Restrictions

3. Newly amended claim 29 is directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: it is drawn to a method of determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product, wherein the method occurs in vivo. This is a distinct and independent invention from that originally elected, and is encompassed by Group III in the restriction mailed June 10, 1999.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claim 29 will only be examined in so far as it is directed to an in vitro method. See 37 CFR 1.142(b) and MPEP § 821.03.

Sequence Compliance

4. The communication filed January 27, 2003 is not fully responsive to the Office communication mailed August 7, 2002 for the reason(s) set forth on the CRF Diskette Problem Report. Applicant must comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825) before the application can be examined under 35 U.S.C. §§ 131 and 132.

Since the reply appears to be bona fide attempt to comply with the requirements of the sequence rules (37 CFR 1.821 - 1.825), applicant is given the statutory time from the mailing date of this communication within which to correct the deficiency so as to comply with the sequence rules (37 CFR 1.821 - 1.825) in order to avoid abandonment of the application under 37 CFR 1.821(g). EXTENSIONS OF THIS TIME PERIOD MAY BE GRANTED UNDER 37 CFR 1.136(a).

Applicant is reminded that the CRF should NOT be sent to the 20231 zip code address for the United States Patent and Trademark Office, because mail sent there is irradiated, and instead should be sent via the following to the indicated addresses listed on the bottom of the CRF Problem Report.

Withdrawn Rejections

5.1 The rejection of claim 4 under 35 USC § 103 is withdrawn in view of Applicants' reply and the declaration filed June 24, 2002.

5.2 The rejection of claim 29 under 112 § 1 is withdrawn in view of Applicants' amendment.

Claim Objections

6. Claim 29 is objected to because of the following informalities: it encompasses a non-elected invention. Appropriate correction is required.

Maintained Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 11 and 12 remain rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product (RAGE) in a competitive assay using a peptide that is a carboxyl-lysine-modified AGE, does not reasonably provide enablement for a peptide derivative comprising an alkyl group. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims, for reasons of record in the previous Office Actions, Paper No. 11 at pages 3-4, Paper No. 13 at pages 2-4, and Paper No. 18.

Claims 11 and 12 encompass the competitive binding assay of claim 1, in which the peptide derivative of step (a) (i) comprises an alkyl derivative, which can be an acetyl derivative, a propyl derivative, an isopropyl derivative, a butyl derivative, an isobutyl derivative, or a carboxymethyl derivative. The specification teaches a number of experiments that were performed to elucidate the specific binding of AGE peptides to a RAGE, or the effects of these AGE peptides on various cell types (Figures 1-7 and pages 4-6 of the specification). However, the only AGEs that were used in these experiments were carboxyl-lysine (CML), pentosidine, and methylglyoxal modified proteins. In Figure 1 and in the Brief Description of the Drawings

on page 4 and the results section on pages 33-34, it was demonstrated that in the radioligand binding assays in which CML-BSA, pentosidine-BSA or methylglyoxal-human serum albumin were tested, only CML-BSA specifically bound to RAGE. Both pentosidine-BSA and methylglyoxal-HSA did not bind specifically to RAGE. Similar results were found in the other experiments shown in Figures 2-7 and in the results section. The rejection of claims 11 and 12 under 35 USC 112, first paragraph, limited to the peptide derivative being an alkyl derivative, is maintained, because although Applicant on page 3 of the amendment filed June 24, 2002, Paper No. 16, demonstrates that the methyl group of carboxymethly-lysine is an alkyl group, the specification also teaches that methylglyoxal-HSA did not bind specifically to RAGE (pages 33-34 of specification). Therefore, one of ordinary skill in the art would not expect any alkyl derivative AGE would bind to RAGE. The prior art does not disclose that peptides comprising an alkyl derivative are AGEs, or that they would bind to RAGE.

It is not disclosed and not predictable from the limited teachings of the prior art and specification that any peptide comprising an alkyl derivative would bind to a RAGE and function in a competitive binding assay, as claimed. It is not predictable, based on the information provided in the specification or from the prior art, that the claimed compositions could be used in such assays, especially in light of the experimental results that teach that only the carboxymethly-lysine-modified peptide specifically bound to RAGE. The specification has not provided the person of ordinary skill in the art the guidance necessary to be able to use a peptide comprising any alkyl derivative in the assay as claimed. Therefore, the method of using such derivatives is not enabled.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

8. Claims 1, 2, 5-8, 13, 15, 17, 18, 20-22 and 24-28 remain rejected, and claim 29 is now rejected, under 35 U.S.C. 102(e) as being anticipated by Morser et al., PN 5,864,018, filing date April 16, 1996, for reasons cited in the previous Office Actions, Paper No. 9, at pages 6-8 and Paper No. 13, at pages 5-6.

Claims 1, 2, 5-8, 13, 15, 17, 18, 20-22 and 24-29 encompass a method for determining whether a compound is capable of inhibiting the interaction of a peptide with a receptor for advanced glycation end product (RAGE) in a competitive assay, comprising admixing the peptide (wherein the amino groups are inactivated by chemical derivatization) with RAGE or a fragment of RAGE in the presence and the absence of the compound, wherein the peptide is an AGE or fragment thereof that is carboxymethly-lysine, modified, synthetic, the peptide is derivatized via chemical modification resulting in an alkyl derivative or is synthetic, and wherein the RAGE or RAGE fragment is synthetic, soluble or comprises the V-domain, wherein the compound is sRAGE, a polypeptide, a polyclonal or monoclonal, humanized, chimeric or privatized antibody, and wherein the peptide or RAGE is affixed to a solid surface, and the peptide or RAGE is labeled.

Morser et al. teach a method of using the AGE/RAGE interaction in order to screen test compounds in order to identify agonists or antagonists of the AGE/RAGE interaction. In column 16, line 29 to column 17, line 54, Morser et al. teaches that test compounds may be chemical compounds, biological macromolecules, or extracts made from biological materials such as bacteria, plants, fungi, or animal cells or tissues, and test compounds will typically include the polypeptides or fragments of the present invention (AGEs and RAGE or sRAGE or RAGE fragment) as well as structural analogs or peptidomimetics which are derived from these polypeptides or the antibodies described in the patent, and substrates or ligands thereof (column 16, lines 35-44).

In column 16, line 50 to column 17, line 35, Morser et al. teach that the screening methods typically involve incubation of RAGE with an advanced glycoslylation end-product protein (AGE, a derivatized, inactivated protein) such as AGE-BSA, nonenzymatically N-glycosylated collagen, myelin or the like, as well as the test compound, and that typically, one of the RAGE polypeptide or AGE will be immobilized upon a solid support which will then be contacted with the other protein or peptide, and that the one of the pair will include a labeling group such as radiolabels, chemiluminescent or fluorescent groups (column 9, lines 44-54).

In column 5, lines 24-28, Morser et al. teach that the soluble RAGE polypeptides generally comprise fragments of the extracellular domain of RAGE, and the soluble peptides will comprise one or more of the IG-like domains of the extracellular region of RAGE (the V-domain). In column 6, lines 41-52, Morser et al. also teach that the polypeptides may also be characterized by their ability to block the interaction between two proteins, and include peptides

derived from RAGE such as fragments which encompass AGE binding regions of RAGE as well as AGE-binding proteins.

In column 5, lines 33-38, Morser et al. teach that the polypeptides may be characterized by their ability to either mimic or inhibit the interaction between AGEs and their receptors (RAGE), and that those polypeptides which are mimetic of either AGE or its receptors in the AGE/receptor interaction are termed AGE or AGE receptor "mimics".

Morser et al. in column 10, line 6 to column 11, line 56 teach antibodies that bind with relative high affinity to RAGE, and can be used for a number of purposes, including inhibiting interaction between AGEs and their receptors, and that these antibodies can be monoclonal, polyclonal, fragments, chimeric or humanized. In column 7, lines 22-35, Morser et al. teaches that the polypeptides of the invention may be prepared using synthetic methods. Morser et al., in column 21, Example 2, describes the preparation of AGE-BSA, by incubating bovine serum albumin with ribose in the presence of PMSF. This is a chemical derivatization, and though Morser et al. does not specifically state that the amino groups of the BSA are less reactive with the chemical modification than without such chemical modification, this is inherent property of such a derivatized protein. Therefore, this modified peptide meets the limitations of the claims, and the rejection of claims under 35 USC § 102(e) is maintained.

Therefore, from the teachings of Morser et al., claims 1, 2, 5-8, 11-13, 15, 17, 18, 20-22 and 24-29 are anticipated.

Conclusion

9.1 Claim 4 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

9.2 Claims 1, 2, 5-8, 11-13, 15, 17, 18, 20-22 and 24-29 are rejected.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eileen B. O'Hara, whose telephone number is (703) 308-3312. The examiner can normally be reached on Monday through Friday from 10:00 AM to 6:30 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached at (703) 308-6564.

Official papers Before Final filed by RightFax should be directed to (703) 872-9306.

Official papers After Final filed by RightFax should be directed to (703) 872-9307.

Official papers filed by fax should be directed to (703) 308-4242.

Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Eileen B. O'Hara, Ph.D.

Patent Examiner

LORRAINE SPECTOR
PRIMARY EXAMINER

Notice to Comply	Application No.	Applicant(s)	
	09/166,649	Schmidt et al.	
	Examiner	Art Unit	
	Eileen B. O'Hara	1646	

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☒ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☐ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☒ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☐ 7. Other:

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☐ An initial or substitute paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216
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